

Genes & Development**Using Antibodies:
A Laboratory Manual****NEW! Molecular Cloning:
A Laboratory Manual, Third Edition**[HOME](#) [HELP](#) [FEEDBACK](#) [SUBSCRIPTIONS](#) [ARCHIVE](#) [SEARCH](#) [TABLE OF CONTENTS](#)Institution: [US PATENT & TRADEMARK OFFICE](#) || [Sign In as Individual](#) ||[Contact Subscription Administrator at your institution](#) || [FAQ](#)

Genes & Development, Vol 10, 165-175, Copyright © 1996 by Cold Spring Harbor Laboratory Press

RESEARCH PAPERS

Keratinocyte growth factor is required for hair development but not for wound healing

L Guo, L Degenstein and E Fuchs

Howard Hughes Medical Institute, Department of Molecular Genetics and Cell Biology, University of Chicago, Illinois 60637, USA.

Keratinocyte growth factor (KGF), also known as fibroblast growth factor 7 (FGF7), is synthesized by skin fibroblasts. However, its mitogenic activity is on skin keratinocytes, where it is the most potent growth factor identified thus far. To explore KGF's function in vivo, we used embryonic stem cell technology to generate mice lacking KGF. Over time, their fur developed a matted appearance, very similar to that of the rough mouse, whose recessive mutation maps at or near the KGF locus on mouse chromosome 2. In contrast to the recently reported transforming growth factor- α (TGF- α) and FGF5 knockouts, which showed defects in the follicle outer-root sheath and the hair growth cycle, respectively, the hair defect in the KGF knockout seemed to be restricted to the cells giving rise to the hair shaft. Thus, we have uncovered a third, and at least partially nonoverlapping, growth factor pathway involved in orchestrating hair follicle growth and/or differentiation. Surprisingly, the absence of KGF resulted in no abnormalities in epidermal growth or wound healing. This was true even when we engineered double knockout mice, null for both KGF and TGF- α , two factors that are increased dramatically in the normal wound-healing process. Whereas we found no evidence of compensatory changes at the mRNA level of wounded knockout mice, these data imply that the regulation of epidermal growth is complex and involves a number of growth stimulatory factors that go beyond what are thought to be the major paracrine and autocrine growth factors. We suggest that the redundancy in epidermal growth and wound healing is likely to stem from the vitality of these functions to the organism, a feature that is not a consideration for the hair follicle.

This article has been cited by other articles:

- Martin, P. (1997). Wound Healing--Aiming for Perfect Skin Regeneration. *Science* 276: 75-81
[\[Abstract\]](#) [\[Full Text\]](#)
- Wang, Z., Tufts, R., Haleem, R., Cai, X. (1997). Genes regulated by androgen in the rat

- ▶ Similar articles found in:
[Genes Dev. Online](#)
[PubMed](#)
- ▶ [PubMed Citation](#)
- ▶ Search Medline for articles by:
[Guo, L](#) || [Fuchs, E](#)
- ▶ Alert me when:
new articles cite this article
- ▶ [Download to Citation Manager](#)

- ventral prostate. *Proc. Natl. Acad. Sci. U. S. A.* 94: 12999-13004 [Abstract] [Full Text]
- Ortega, S., Ittmann, M., Tsang, S. H., Ehrlich, M., Basilico, C. (1998). Neuronal defects and delayed wound healing in mice lacking fibroblast growth factor 2. *Proc. Natl. Acad. Sci. U. S. A.* 95: 5672-5677 [Abstract] [Full Text]
 - Gimond, C., Baudoin, C., van der Neut, R., Kramer, D., Calafat, J., Sonnenberg, A. (1998). Cre-loxP-mediated Inactivation of the alpha 6A Integrin Splice Variant In Vivo: Evidence for a Specific Functional Role of alpha 6A in Lymphocyte Migration but Not in Heart Development. *J. Cell Biol.* 143: 253-266 [Abstract] [Full Text]
 - Resnick, J. L., Ortiz, M., Keller, J. R., Donovan, P. J. (1998). Role of Fibroblast Growth Factors and Their Receptors in Mouse Primordial Germ Cell Growth. *Biol Reprod* 59: 1224-1229 [Abstract] [Full Text]
 - Bajaj-Elliott, M., Poulson, R., Pender, S. L.F., Wathen, N. C., MacDonald, T. T. (1998). Interactions between Stromal Cell- derived Keratinocyte Growth Factor and Epithelial Transforming Growth Factor in Immune-mediated Crypt Cell Hyperplasia. *J. Clin. Invest.* 102: 1473-1480 [Abstract] [Full Text]
 - van Steensel, M. A. M., Happel, R., Steijlen, P. M. (2000). Molecular Genetics of the Hair Follicle: The State of the Art. *EXP BIOL MED* 223: 1-7 [Abstract] [Full Text]
 - Igarashi, M., Finch, P. W., Aaronson, S. A. (1998). Characterization of Recombinant Human Fibroblast Growth Factor (FGF)-10 Reveals Functional Similarities with Keratinocyte Growth Factor (FGF-7). *J. Biol. Chem.* 273: 13230-13235 [Abstract] [Full Text]
 - Ahmad, W., Faiyaz ul Haque, M., Brancolini, V., Tsou, H. C., ul Haque, S., Lam, H., Aita, V. M., Owen, J., deBlaquiere, M., Frank, J., Cserhalmi-Friedman, P. B., Leask, A., McGrath, J. A., Peacocke, M., Ahmad, M., Ott, J., Christiano, A. M. (1998). Alopecia Universalis Associated with a Mutation in the Human *hairless* Gene. *Science* 279: 720-724 [Abstract] [Full Text]
 - ARANY, E., HILL, D. J. (2000). Ontogeny of Fibroblast Growth Factors in the Early Development of the Rat Endocrine Pancreas. *Pediatr Res* 48: 389-403 [Abstract] [Full Text]
 - Bikfalvi, A., Klein, S., Pintucci, G., Rifkin, D. B. (1997). Biological Roles of Fibroblast Growth Factor-2. *Endocr Rev* 18: 26-45 [Abstract] [Full Text]
 - ROTH, W., DEUSSING, J., BOTCHKAREV, V. A., PAULY-EVERS, M., SAFTIG, P., HAFNER, A., SCHMIDT, P., SCHMAHL, W., SCHERER, J., ANTON-LAMPRECHT, I., VON FIGURA, K., PAUS, R., PETERS, C. (2000). Cathepsin L deficiency as molecular defect of furless: hyperproliferation of keratinocytes and perturbation of hair follicle cycling. *FASEB J.* 14: 2075-2086 [Abstract] [Full Text]
 - Hom, Y. K., Young, P., Thomson, A. A., Cunha, G. R. (1998). Keratinocyte Growth Factor Injected into Female Mouse Neonates Stimulates Uterine and Vaginal Epithelial Growth. *Endocrinology* 139: 3772-3779 [Abstract] [Full Text]
 - Sano, S., Kira, M., Takagi, S., Yoshikawa, K., Takeda, J., Itami, S. (2000). Two distinct signaling pathways in hair cycle induction: Stat3-dependent and -independent pathways. *Proc. Natl. Acad. Sci. U. S. A.* 10.1073/pnas.240303097v1 [Abstract] [Full Text]
 - Escalante-Alcalde, D., Recillas-Targa, F., Valencia, C., Santa-Olalla, J., Chávez, P., Marroquín, A., Gutiérrez-X, L., Gariglio, P., Covarrubias, L. (2000). Expression of E6 and E7 Papillomavirus Oncogenes in the Outer Root Sheath of Hair Follicles Extends the Growth Phase and Bypasses Resting at Telogen. *Cell Growth Differ* 11: 527-539 [Abstract] [Full Text]
 - Cardoso, W. V. (2001). MOLECULAR REGULATION OF LUNG DEVELOPMENT. *Annu. Rev. Physiol.* 63: 471-494 [Abstract] [Full Text]
 - Clark, J. C., Tichelaar, J. W., Wert, S. E., Itoh, N., Perl, A.-K. T., Stahlman, M. T., Whitsett, J. A. (2001). FGF-10 disrupts lung morphogenesis and causes pulmonary adenomas in vivo. *Am. J. Physiol.* 280: 705L-715 [Abstract] [Full Text]
 - Shannon, J. M., Pan, T., Nielsen, L. D., Edeen, K. E., Mason, R. J. (2001). Lung Fibroblasts Improve Differentiation of Rat Type II Cells in Primary Culture. *Am J Respir Cell Mol Biol* 24:

235-244 [\[Abstract\]](#) [\[Full Text\]](#)

- Chelly, N., Henrion, A., Pinteaur, C., Chailley-Heu, B., Bourbon, J. R. (2001). Role of Keratinocyte Growth Factor in the Control of Surfactant Synthesis by Fetal Lung Mesenchyme. *Endocrinology* 142: 1814-1819 [\[Abstract\]](#) [\[Full Text\]](#)
- Fassett, J. T., Nilsen-Hamilton, M. (2001). Mrp3, a Mitogen-Regulated Protein/Proliferin Gene Expressed in Wound Healing and in Hair Follicles. *Endocrinology* 142: 2129-2137 [\[Abstract\]](#) [\[Full Text\]](#)
- Celli, G., LaRochelle, W. J., Mackem, S., Sharp, R., Merlino, G. (1998). Soluble dominant-negative receptor uncovers essential roles for fibroblast growth factors in multi-organ induction and patterning. *EMBO J.* 17: 1642-1655 [\[Abstract\]](#) [\[Full Text\]](#)
- Min, H., Danilenko, D. M., Scully, S. A., Bolon, B., Ring, B. D., Tarpley, J. E., DeRose, M., Simonet, W. S. (1998). Fgf-10 is required for both limb and lung development and exhibits striking functional similarity to *Drosophila* branchless. *Genes & Dev.* 12: 3156-3161 [\[Abstract\]](#) [\[Full Text\]](#)
- Dai, X., Schonbaum, C., Degenstein, L., Bai, W., Mahowald, A., Fuchs, E. (1998). The ovo gene required for cuticle formation and oogenesis in flies is involved in hair formation and spermatogenesis in mice. *Genes & Dev.* 12: 3452-3463 [\[Abstract\]](#) [\[Full Text\]](#)
- Chelly, N., Mouhieddine-Gueddiche, O.-B., Barlier-Mur, A.-M., Chailley-Heu, B., Bourbon, J. R. (1999). Keratinocyte Growth Factor Enhances Maturation of Fetal Rat Lung Type II Cells. *Am J Respir Cell Mol Biol* 20: 423-432 [\[Abstract\]](#) [\[Full Text\]](#)
- Miller, D. L., Ortega, S., Bashayan, O., Basch, R., Basilico, C. (2000). Compensation by Fibroblast Growth Factor 1 (FGF1) Does Not Account for the Mild Phenotypic Defects Observed in FGF2 Null Mice. *Mol. Cell. Biol.* 20: 2260-2268 [\[Abstract\]](#) [\[Full Text\]](#)
- Booth, C., Potten, C. S. (2000). Keratinocyte Growth Factor Increases Hair Follicle Survival Following Cytotoxic Insult. *J Invest Dermatol* 114: 667-673 [\[Abstract\]](#) [\[Full Text\]](#)
- Parrott, J. A., Skinner, M. K. (1998). Developmental and Hormonal Regulation of Keratinocyte Growth Factor Expression and Action in the Ovarian Follicle. *Endocrinology* 139: 228-235 [\[Abstract\]](#) [\[Full Text\]](#)
- Botchkarev, V. A., Komarova, E. A., Siebenhaar, F., Botchkareva, N. V., Sharov, A. A., Komarov, P. G., Maurer, M., Gudkov, A. V., Gilchrist, B. A. (2001). p53 Involvement in the Control of Murine Hair Follicle Regression. *Am J Pathol* 158: 1913-1919 [\[Abstract\]](#) [\[Full Text\]](#)
- Miralles, F., Czernichow, P., Ozaki, K., Itoh, N., Scharfmann, R. (1999). Signaling through fibroblast growth factor receptor 2b plays a key role in the development of the exocrine pancreas. *Proc. Natl. Acad. Sci. U. S. A.* 96: 6267-6272 [\[Abstract\]](#) [\[Full Text\]](#)
- Tichelaar, J. W., Lu, W., Whitsett, J. A. (2000). Conditional Expression of Fibroblast Growth Factor-7 in the Developing and Mature Lung. *J. Biol. Chem.* 275: 11858-11864 [\[Abstract\]](#) [\[Full Text\]](#)
- Sano, S., Kira, M., Takagi, S., Yoshikawa, K., Takeda, J., Itami, S. (2000). Two distinct signaling pathways in hair cycle induction: Stat3-dependent and -independent pathways. *Proc. Natl. Acad. Sci. U. S. A.* 97: 13824-13829 [\[Abstract\]](#) [\[Full Text\]](#)
- Paus, R., Cotsarelis, G. (1999). The Biology of Hair Follicles. *N Engl J Med* 341: 491-497 [\[Full Text\]](#)
- Stenn, K. S., Paus, R. (2001). Controls of Hair Follicle Cycling. *Physiol. Rev* 81: 449-494 [\[Abstract\]](#) [\[Full Text\]](#)
- Maatta, A., Jaakkola, P., Jalkanen, M. (1999). Extracellular Matrix-dependent Activation of Syndecan-1 Expression in Keratinocyte Growth Factor-treated Keratinocytes. *J. Biol. Chem.* 274: 9891-9898 [\[Abstract\]](#) [\[Full Text\]](#)
- Zieske, J. D., Takahashi, H., Hutcheon, A. E. K., Dalbone, A. C. (2000). Activation of Epidermal Growth Factor Receptor during Corneal Epithelial Migration. *Invest. Ophthalmol. Vis. Sci.* 41: 1346-1355 [\[Abstract\]](#) [\[Full Text\]](#)
- ANDREADIS, S. T., HAMOEN, K. E., YARMUSH, M. L., MORGAN, J. R. (2001). Keratinocyte

growth factor induces hyperproliferation and delays differentiation in a skin equivalent model system. *FASEB J.* 15: 898-906 [[Abstract](#)] [[Full Text](#)]

- Krakowski, M. L., Kritzik, M. R., Jones, E. M., Krah, T., Lee, J., Arnush, M., Gu, D., Sarvetnick, N. (1999). Pancreatic Expression of Keratinocyte Growth Factor Leads to Differentiation of Islet Hepatocytes and Proliferation of Duct Cells. *Am J Pathol* 154: 683-691 [[Abstract](#)] [[Full Text](#)]
- Emoto, H., Tagashira, S., Mattei, M.-G., Yamasaki, M., Hashimoto, G., Katsumata, T., Negoro, T., Nakatsuka, M., Birnbaum, D., Coulier, F., Itoh, N. (1997). Structure and Expression of Human Fibroblast Growth Factor-10. *J. Biol. Chem.* 272: 23191-23194 [[Abstract](#)] [[Full Text](#)]
- Hajihosseini, M. K., Wilson, S., De Moerloose, L., Dickson, C. (2001). A splicing switch and gain-of-function mutation in FgfR2-IIIc hemizygotes causes Apert/Pfeiffer-syndrome-like phenotypes. *Proc. Natl. Acad. Sci. U. S. A.* 98: 3855-3860 [[Abstract](#)] [[Full Text](#)]
- Colvin, J. S., White, A. C., Pratt, S. J., Ornitz, D. M. (2001). Lung hypoplasia and neonatal death in Fgf9-null mice identify this gene as an essential regulator of lung mesenchyme. *Development* 128: 2095-2106 [[Abstract](#)] [[Full Text](#)]
- Revest, J.-M., Suniara, R. K., Kerr, K., Owen, J. J. T., Dickson, C. (2001). Development of the Thymus Requires Signaling Through the Fibroblast Growth Factor Receptor R2-IIIb. *The JI* 167: 1954-1961 [[Abstract](#)] [[Full Text](#)]
- Lund, L. R., Rømer, J., Bugge, T. H., Nielsen, B. S., Frandsen, T. L., Degen, J. L., Stephens, R. W., Danø, K. (1999). Functional overlap between two classes of matrix-degrading proteases in wound healing. *EMBO J.* 18: 4645-4656 [[Abstract](#)] [[Full Text](#)]

[HOME](#) [HELP](#) [FEEDBACK](#) [SUBSCRIPTIONS](#) [ARCHIVE](#) [SEARCH](#) [TABLE OF CONTENTS](#)

[GENOME RESEARCH](#)

[LEARNING & MEMORY](#)

[PROTEIN SCIENCE](#)

[GENES & DEVELOPMENT](#)